strategy+business

Gary Pisano: The Thought Leader Interview

by Amy Bernstein

from **strategy+business** issue 47, Summer 2007

reprint number 07210

Reprint

Photograph by Steven Edson

Gary Pisano: The Thought Leader Interview

A leading student of the biotech business describes the problems holding the industry back, and how it can overcome them.

by Amy Bernstein

Over the last two decades, Harvard Business School professor Gary Pisano has been grappling with the central disappointment of biotechnology. The industry has consistently fallen short of its promise to improve human health, he says, because the goals and requirements of science and those of business often conflict. Businesses, particularly public companies, are in a quarterly race to show financial gains, while science demands long-term inquiry. Thus, according to Pisano, the organizational structures and business models that dominate the biotech industry are inappropriate to its scientific objectives.

Pisano's research bears this out. His analysis of financial reports from publicly held biotech companies shows that the industry as a whole has lost money, even though revenues grew exponentially over the course of the 20-year period that he studied. Given that public companies in a particular sector are generally in better financial shape than their private counterparts, the industry's results as a whole have probably been even bleaker.

But his analysis yielded a bigger

Amy Bernstein
(bernstein_amy@strategy-business.com) is deputy editor of *strategy+business*.

surprise: Biotech's R&D productivity was nowhere near what was expected. Experts watching this industry have assumed from the beginning that biotech R&D productivity would outpace that of pharmaceuticals. After all, most biotech firms are still entrepreneurial and agile, unencumbered by the bureaucracies of large pharma companies. Pisano found that, in fact, biotech R&D performance was no better than that of pharma.

Understanding why biotech has failed to reach its potential has become Pisano's mission. His first book, *The Development Factory: Unlocking the Potential of Process Innovation* (Harvard Business School Press, 1996), examined strategies for improving development performance in biotech and pharmaceuticals. His more recent book, *Science Business: The Promise, the Reality, and the Future of Biotech* (Harvard Business School Press, 2006), examines the biotech industry's inherent dissonance and proposes ways to reconcile its business goals with its scientific goals. He posits that the field will hit its stride only when it engenders companies with a new capacity for alliances, big-bet investments, and long-term planning. On a blustery December morning in Boston, Mass., Gary Pisano, Harvard University's Harry E. Figgie Jr. Professor of Business Administration, sat down in his office to discuss his insights with *strategy+business.*

S+B: Describe the promise of biotech as an industry and why you say it has fallen short.

PISANO: Biotech opens up opportunities for different kinds of businesses to enter the pharmaceutical industry, essentially disrupt it, and become very profitable enterprises. But that promise has not yet been fully realized.

There are a couple of reasons for this. One is that expectations were way too high. Investors and entrepreneurs failed to understand what's really required for a science-based business to take off. More specifically, the business's structure and certain long-term assumptions about it have led to an industry anatomy that is inconsistent with the requirements of the science. In any science-based business, the nature of the science should determine in large part the design of the business models, organizational structures, and institutional arrangements. But in biotech, that's not the case. Look in depth at the science of biotech — I use that term broadly to mean the whole constellation of new tools, technologies, and techniques for drug discovery that have evolved over the last 30 years — and consider the business problems that science creates.

Let's start with the first: risk. Drug development is hampered by profound and persistent uncertainty. Developing a drug involves coming up with a component that goes into the human body. But drug development is different from the many other processes that develop components to go into systems. A chip maker, for example, knows all about the system his product has to fit. But our knowledge of human biological systems and processes is limited; we understand pieces of the system but not the entirety of it. Unlike chips and computers, the human body's operating system is not well specified and not yet fully documented. Furthermore, every body's "system" is different. And there's no way to adjust related subsystems — the way chip designers do — to accommodate the component in question. Certain things work; certain things don't. The drug

development process is still very much trial and error. We're dealing with constraints that you just don't see in other kinds of businesses.

The second problem is a basic misunderstanding about "the biotech revolution." It's not a single revolution. It's a constellation of revolutions in such fields as mathematics, biology, molecular biology, genomics, bioinformatics, and software. The power to impact drug discovery lies in how you integrate the understanding and the tools. You can't just say, "Here's a new advance. This solves all the problems." You have to evaluate how each new tool works in relation to all the others. You have to bring all the tools and knowledge together.

The third challenge involves the cumulative advance of knowledge. Unlike knowledge in other businesses, where the new drives out the old, in biotech the new gets layered on top of the old, and the old stuff stays relevant. In drugs, ideas and discoveries that are 100 years old are often still relevant today. And the skills you needed to develop drugs 20 years ago are still the skills you need today. So you need to keep extending the frontier of understanding.

So those are the three challenges created by the science of biotech: You've got to be able to manage risk to deal with uncertainty, you've got to be able to achieve integration across all the separate areas that constitute biotech, and you've got to be able to learn rapidly and keep up with the cumulative advances. How would you want the business to look to achieve those goals? You wouldn't want it to look the way it does today. Its anatomy has not evolved to solve those problems.

S+B: Describe the disconnect. How are the three structural requirements not being met?

PISANO: The industry has evolved essentially to manage risk — one of those problems I mentioned — and that's given rise to three forces that shape the way the industry has developed and does business.

First, it creates a lot of new enterprises, usually by using venture capital to spin them off from universities. This approach produces numerous small, specialized companies that are very entrepreneurial. It creates high risk at the firm level but just the opposite at the full industry level. In other words, we deal with risk in this industry by running a lot of experiments, and rewarding entrepreneurs for taking risks at the expense of the longevity of their companies. We've reduced risk by allowing firms to go public at fairly early stages, using equity funding to diversify more uniformly across the portfolio. Although it's important to get science out of the labs and into commercial practice, this approach is not the best way to organize R&D-centric knowledge businesses like biotech.

The problem is that every new idea gets its own firm. Venture investors are ready to write a check every time somebody comes up with a scientifically interesting concept that is at best years away from becoming a drug. That leads to a proliferation of firms and a highly fragmented industry. And every time you launch a new firm, you start the learning cycle all over again. The main downside to an industry composed of many small enterprises operating independently is that the fragmentation cuts directly against all the things we'd want to do to support integration and cumulative learning. I'm not saying entrepreneurialism is a bad thing, but it can go too far.

So by solving the first problem — dealing with risk — we make it harder to solve the second and third problems: integration and the cumulative advance of knowledge.

S+B: The industry, then, is constantly in startup mode.

PISANO: The funding models are the problem; that's the second force undermining the long-term interests of biotech. This industry uses the classic venture funding approach, which has worked extremely well for launching firms in software, semiconductors, and other high-tech realms. Because it provides very close governance, venture capital (VC) is great for early-stage firms. The problem is that it's inappropriate for a business in which it takes 10 years and a billion dollars to bring a new drug to market. Most venture capitalists think in three-year time horizons and, because they need to diversify their own risks, they'd never invest a billion dollars in a single company. They need an exit strategy, and their strategy of choice has long been the public equity market because that's where you get the big payoffs. So public equity solves one problem by paying back investors and allowing the shareholders to diversify.

But public equity was never designed for an R&D enterprise, because the markets don't know how to value R&D. Standard accounting and financial methodologies don't really address the value of intangible assets like R&D, and the generally accepted accounting principles (GAAP) don't require disclosure of R&D portfolios. Also, although pharma and biotech companies must disclose information on their development pipelines, the amount of detail they reveal varies widely from one company to the next. As an investor, you really need somebody on the inside who understands the science; public equity isn't set up to do that.

S+B: Given VC's shorter time horizons, how do the investors get their money back in a business where it takes a decade to go from blackboard to market?

PISANO: That gets us to the third troubling dynamic: the drive to monetize intellectual property (IP). Again, it's worked very well elsewhere, but it's problematic in biotech. Start with the understanding that it's nearly impossible for a firm to get a billion dollars in funding for the decade-long process of developing a drug for market. So early in the life of this industry, entrepreneurs and venture capitalists came up with the idea of monetizing IP by selling it off. You come up with a concept, get it rolling, find a corporate partner, and capitalize via an alliance, a licensing fee, or future royalties, among other options. Monetizing IP occurs all over the place — in the book business, music, software, electronics. In those industries, the market for know-how is vigorous, and the system functions well.

But in biotech, knowledge is not easily tradable. Monetization of intellectual property works really well when you have modularized ideas contained clearly in formats — for example, written code — that are easily transferable and that can work like puzzle pieces or links in a chain. But biotech involves plenty of tacit knowledge that's interwoven with other elements of the system. There is a lot of science in biotech, but also a lot of art. Drug development is a messy process and involves judgments based on both hard scientific data and the researchers' individual experience. It's very difficult to transfer

> **"In most pharma–biotech alliances, the longer-term, value-creating relationship never has a chance to blossom."**

this type of knowledge from one organization to another because researchers have different skills and different experiences. The market for know-how is not an efficient way to get lots of different players together in biotech.

Many have suggested that this business should work like the movie industry, but it can't. For a movie, the studio hires the needed inputs — producers, directors, actors, costumers, camera operators, and so forth — to come together and produce the film. Why can't you do that here? Because there's a well-understood technology for making films. If I'm a cameraperson, I know exactly what I have to do. And if I'm a cameraperson for your movie today, I can be a cameraperson on someone else's movie tomorrow. It always works the same way.

But knowledge in biotech is not fungible. It's highly specific. The monetization of intellectual property assumes that we can buy and sell knowledge as if it's a commodity and find different partners. Biotech is too complex a system for monetization of IP to work. And monetizing IP this way cuts directly against the impetus toward integration. If firms truly believe they can profit by focusing on just one piece of the puzzle, they become myopic. They will build their own island of expertise, and fail to consider how their approach links with others.

Diverging Innovation

S+B: You've identified a disconnect between the paths of innovation in business and science. What does that reveal about the biotech sector?

PISANO: There are two types of innovation required here. One is scientific innovation, which we see all over the place. The second is innovation in business models and approaches. That's what Alfred Chandler, the great business historian, was getting at when he noted that the railroads would not have been possible without the creation of the modern corporation. Before railroads, there weren't corporations. But then railroads required a large amount of capital, and that meant raising money from other sources. That in turn required separating ownership from management. Venture capital moved along a similar path, evolving in the 1940s and '50s and '60s as an institutional innovation to enable the funding of small companies.

In this new epoch of science-based businesses, what organizational and business innovations will enable scientific innovation? Consider again the funding models. As I noted, there are problems with venture capital. And public equity isn't ideal for this business either, not only because of the disclosure issues, but because the market demands quarterly growth, and that's a tall order for an industry in which new product development can take 10 years or longer. Private equity firms are now getting involved with more mature firms in the sector, and they're starting to transform the models, at least for the middle stages between venture capital and public equity. Just how that will play out is yet to be seen.

We're also seeing the rise of the quasi-public firm, which preserves the benefits of public equity while mitigating its downside. These firms are publicly traded, but the majority of their stock is held by a corporate partner. Genentech is a good example; the Swiss pharmaceutical giant Hoffmann–La Roche owns 60 percent of its equity. This gives Genentech the oversight of an informed investor and the financial support it needs to pursue long-

"You don't have to have giant, fully integrated firms, but you can't have an industry largely made up of scads of new firms."

term R&D strategies, without needing to show quarterly growth. Another advantage is that by having stock that floats, even if it's a minority of the shares, you still have an incentive to attract and keep talent. Still, despite the success of the alliance between Genentech and La Roche, there's always a danger that the oversight arrangement can become confining to the biotech entity if the bigger partner gets too meddlesome.

More important, the Genentech example is the exception rather than the rule. Right now most pharma companies manage alliances with biotech firms in such a way as to diversify their risk. They enter into 40 such arrangements and they don't really care which ones work, just as long as at least a few do. The contracts are usually for just four years on average. And the relationships are often fraught because the contracts are usually geared toward specific, short-term milestones. A longer-term, value-creating relationship never has a chance to blossom. In addition, these loose arrangements don't yield the integration that's so necessary for real progress. You don't get the long-term learning between the two partners that is the essence of true collaboration.

Meanwhile, we're seeing a rise in venture philanthropy — funding for specialized research from not-for-profit institutions like the Bill and Melinda Gates Foundation, Michael Milken's Prostate Cancer Foundation, Steve Case's Accelerate Brain Cancer Cure, and the Michael J. Fox Foundation for Parkinson's Research. These players exert a good deal of pressure because they're taking some of the most promising new tools, discoveries, and concepts out of the market and placing them in a nonmarket setting. They're run like venture capital organizations in the sense that they use many of the same discipline and oversight approaches as venture capitalists, but their goal is not to maximize the returns for a set of limited partners. Rather, they aim to continue funding the enterprise and its work. That means that their time horizons are much longer than those of a typical VC investor. They also supervise the research, creating networks of collaborators and actively promoting information sharing.

S+B: So you see the funding model moving in a better direction. How about the business model?

PISANO: Biotech has always been an industry in search of a business model that works. The first-generation business model was vertical integration from R&D to marketing. These companies aimed at developing products for market, à la Genentech, whose 1980 IPO was the first for biotech. In those days, even the best-financed public biotech company could afford to support only a few projects without a corporate partner. Even so, the risks were high because each individual project had the power to make or break the company.

By the mid-1980s, as the financial risks of biotech became more apparent, the second generation of biotech startups focused on research and collaborated with established drug companies to develop the products and bring them to market. This allowed the startups to focus on early-stage research, where big pharma was at a disadvantage, and they could form alliances with a number of partners on a number of projects. But this model started running out of steam in the late 1980s, as the pharma companies lost their appetite for early-stage research and looked for programs that were at or near the clinical testing stage.

The third wave followed the launch of the Human Genome Project in 1990. To map all the genes in the human cell, researchers had to process unprecedented quantities of data. This kind of industrialized R&D required all kinds of new software, equipment, and computational horsepower. So the next generation of biotechs were research factories, selling access to their technology platforms, such as genomics, rather than to specific product technologies or therapeutic applications. That approach was wearing itself out by 2001, and now we're back to companies trying to develop products again. We've come full circle.

Integrating for the Future

S+B: Is vertical integration the right model for now?

PISANO: The biotech sector still isn't functioning right. After 30 years of mitigating risk, we need business models that focus more on integration — bringing together the disparate scientific fields, approaches, and skill sets needed to bring a concept to market. I want to see more integrated organizational forms and fewer firms with a broader array of capabilities. They can gather all the relevant technological pieces within their own boundaries, or they can collaborate with outsiders — but very closely, rather than through "alliances" at arm's length. You don't have to have giant, fully integrated firms, but you can't have an industry largely made up of scads of new firms.

The sector needs both large and small companies. Big ones have the means to invest in the science and take on longer-term risks. (Of course, as big firms like Pfizer come under heavier financial pressure, they tend to think in the shorter term, which is a problem.) Think about how great science has been done in corporate settings: It's always at the large companies, like IBM, General Electric, Xerox, and Bell Labs, because science is a long-term proposition and you need excess cash flow to fund it. Larger firms have to be on the vanguard of science. We're seeing that sort of vanguard emerge with firms like Novartis and Merck, which are investing heavily in R&D facilities with the goal of being on the leading edge of something very important for the next 20 to 30 years.

And we'll still need the smaller, independent firms because they provide the entrepreneurial environment and the focus to push the envelope of drug discovery. But they will be much more closely allied with larger companies in terms of their research and development activities. That in itself will require a cultural shift.

S+B: What kind of shift?

PISANO: We have to have recognition among industry leaders and investors that there's a need for more integrated structures and that there are many kinds of viable business models. Some are service businesses — companies that do screening, for example — but they shouldn't become drug developers.

The industry needs to foster lots of collaborators. It might emulate the loose networks of the construction industry and the movie industry, with constantly shifting alliances. Or it might be tighter, like Toyota's network of suppliers. The players form a few long-term alliances that promote knowledge sharing and value creation. If you look at a research area like cancer, hundreds of trials are going on at any given time, and millions of data points are being generated. How can you bring some of that together?

"A big opportunity lurks in one of the great inefficiencies in drug R&D: Most of the valuable information never gets used."

Right now they're all separated, and we're squandering a lot of potential for understanding. Yes, people will publish papers on some of the work, but it's not comprehensive.

On that front, there's a big opportunity lurking in one of the great inefficiencies in drug R&D, which is that most of the valuable information never gets used. When drugs fail in clinical trials — and most do — almost all the data and knowledge generated by the trials is abandoned. Sometimes the company digs deeper into the data to understand what went wrong and apply that insight to another development project. But none of that knowledge from the failures gets shared. Companies repeatedly make the same mistakes as their competitors in the course of the trials and aren't learning from them.

I'd like to see more data sharing at earlier stages of research and development. Maybe clinical trial databases can become public after a year's delay, for example. That's tricky, but such practices have worked in other sectors. When the U.S. semiconductor business was in trouble about two decades ago, having lost its dominance to Japanese firms and the equipment producers, the semiconductor equipment industry formed Sematech, a consortium of 14 U.S. semiconductor manufacturers and the U.S. government, to pool their insight into the market's direction and to share road maps. At the time this was controversial, but it was also a critical factor in helping different parts of the industry build out their capabilities in tandem — and arguably it helped the U.S. semiconductor industry return to growth.

Is there a mechanism to allow firms to share data on the failed projects in a way that would protect their proprietary interests? That one organizational innovation would be a big step toward boosting research and development productivity in both pharma and biotech.

We also need to look at universities. In the last 20 years, universities have become tied up with the idea of creating new firms. It's now very much part of the mission of universities to make sure that their knowledge gets transferred from academia into practice. Sometimes the right way to do that is to create a new firm, but not always. In fact, sometimes the creation of a new firm works against the goal of broad dissemination, because once you take knowledge and put it into a firm, that firm has the IP rights over it, and now you've isolated it there. Universities have to become much more reflective about their position and how they approach their role in sharing knowledge.

S+B: How do we get there from here?

PISANO: Universities could play a role in driving the industry to share clinical knowledge. They could become the disinterested, noncommercial third party that collects the data and disseminates it in a way that's equal and fair to everyone. Or government could play that role, the way it did with the Internet.

One thing that may start to catalyze better information sharing is the rise of China's pharmaceutical industry. If you think about what drove change in other industries, such as semiconductors and autos, it was competition from outside the U.S. But the pharmaceutical industry hasn't had that. Theirs is a global industry, but it has largely been dominated by U.S. and European companies.

There are maybe a couple thousand pharmaceutical companies in China, and they're moving down

the science curve very quickly. What happens if you get a bunch of Chinese companies coming in with very different cost structures, very different organizational structures, doing first-rate science? What happens if some of those companies get their drugs approved in China? And what if those drugs treat diseases like Alzheimer's? Americans are going to demand access to them. That kind of global competition will make the industry take notice and change.

Pharma and biotech are still struggling under their own weight. They can't keep raising prices and they can't keep productivity at the same level. As the problem worsens, some pharma or biotech companies may try to change. For those companies, external competition with new players with very different cost structures could also be an important catalyst.

S+B: As biotech matures, do you see an opportunity for new players, new kinds of businesses?

PISANO: There's lots of room, and that's what is exciting. In the science-based sector you're never quite mature. The industry never quite reaches equilibrium, and that's a good thing.

Are there firms that can truly play the role of integrator? Go back to the movie analogy. A movie is actually a company, its own economic entity. The producer gets the studio to fund it and pulls together all sorts of artists and technicians to make the movie. Everybody gets paid; some people are paid a wage, some are paid a residual. The company is an accounting entity that just hands out checks. And then after production, marketing, and distribution are over, the company goes away. That model assumes that there is a standardized way to do the business. It tends to work with many of the same players over time, and there's a lot of trust that forms because the networks are small.

Similarly, you can imagine a company whose specialty is putting together the pieces for developing drugs. As with the movies, the company calls on players with deep expertise with whom it's worked before — for clinical development, say, it would be the biostatisticians, trial designers, systems analysts, statisticians, and medical doctors, among others. The company is an integrator with a network of ongoing relationships. It gets funding from a variety of sources — private equity, established drug companies — and perhaps it puts in its own money. It taps its network for the best players and it orchestrates the process. No matter whether the effort fails, or succeeds and a drug hits the market, the project disappears when its work is done. The integrator has to be able to pull the plug on an effort if it's not working. There must be an understanding among all the participants that the project can end at any time. And since the risks for the participants are much higher, the incentives for success have to be much higher. You can see how that structure could be very powerful and do much to move the industry closer to its potential as a vital and efficient business that supports — rather than impedes — the progress of science. +

Reprint No. 07210

strategy+business magazine
is published by Booz Allen Hamilton.
To subscribe, visit www.strategy-business.com
or call 1-877-829-9108.

Booz | Allen | Hamilton